DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/31/11 has been entered.

Applicants' Amendment and Response After Final, filed 1/10/11, have been previously entered (see Advisory Action, mailed 1/18/11). Claims 52, 55, 57-75, 78-101 are pending; claims 61-73 are withdrawn; claims 52, 55, 57-60, 74, 75, 78-101 are under current examination.

The Examiner has previously answered Applicants' Arguments, filed in the After-Final Amendment of 1/10/11, in the Advisory Action, mailed 1/18/11. Applicants have not provided any new amendments or remarks accompanying the request for continued examination, filed 1/31/11. The rejections of record stand.

Information Disclosure Statement

Applicants' IDS, filed 1/31/11 has been considered.

Election/Restrictions

Claims 61-73 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/28/08.

Applicant's election of Group I (claims 52, 55-60, 74-74, 78-84) in the reply filed on 11/28/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants further elected SEQ ID NO: 34 for a species election. The Examiner withdraws the species restriction requirement and all species are examined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 52, 55, 58-60, 74, 75, 78-80, 85, 86, 88-94, 99, 100 and 101 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson *et al.* (**Science**, 282: 1145-1147, November 6, 1998, cited previously) in view of Harper (**J. of Assisted Reproduction and Genetics**, 13(2): 90-95, 1996) in further view of US Pat. No. 7,390,659 (Issued June 24, 2008, cited previously) and Elsea *et al.* (**ILAR Journal**, 43(2): 66-79, 2002, cited previously). This rejection is maintained for reasons of record advanced in the prior Office actions (see Advisory Action, mailed 1/18/11; Final Rejection, mailed 7/30/10).

Rejection

Thomson teach human embryonic stem cells from IVF embryos, and teach that genetic modifications could be produced in ES cells, for reducing or combating immune rejection (p. 1147, 1st col). Thomson further teach the production of cell lines from the human ES cells. Thomson teach that human ES cells can be differentiated by allowing the cells to grow to confluence and pile up (production of embryoid bodies, see p. 1146, col. 1, 2nd ¶). Additionally, Thomson teach that human ES cells would be valuable in studies of development and function of tissues that differ between mice and humans, and that screens based upon the *in vitro* differentiation to specific lineages could identify gene targets for new drugs (see p. 1146, col. 2-3, bridging ¶).

Thomson do not specifically teach that the embryos used would have a naturally occurring disease mutation. However, prior to the time of filing, screening of human embryos produced by IVF for various diseases was known in the art. Harper teaches that diseases, such as cystic fibrosis, Lesch Nyhan, Fragile X, Duchenne Muscular Dystrophy, Tay Sachs, haemophilia, can be done by PCR (see p. 1, Materials and Methods. See also pages 91-92, bridging paragraph and Table II. Thus, Harper provides methods in which to identify specific human IVF embryos that have a naturally occurring disease causing mutation in a disease polypeptide, using PCR.

Neither Thomson nor Harper specifically teach the *in vitro* assay steps required by the claims. However, prior to the time of filing, the '659 document teaches methods for identifying candidate agents for treating conditions associated with motor neuron degeneration by obtaining embryonic stem cells, wherein the stem cells contain a mutation in a specific gene, contacting the ES cells with retinoic acid to differentiate the cells into neural progenitor cells, and determining the effect of an agent for use in treatment of a condition associated with motor neuron degeneration. See claim 1.

Given the teachings of Thomson and Harper, one of skill in the art would be able to use the methods of screening human embryos for a specific disease-causing mutation, and use those embryos in the methods taught by Thomson, in order to produce isolated human ES cell lines with a naturally occurring disease-causing mutation, with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to make these types of ES cells in order to use them in *in vitro* assays for identification of targets for new drugs (as suggested by Thomson), or to analyze the molecular mechanisms of the disease by allowing the ES cells to differentiate. Additionally, it would be obvious to utilize the resultant cells in methods of screening agents suitable for treating a disorder, such as the methods taught by the '659 document, with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to make this modification in view of Thomson's teachings who suggest producing genetic modifications in ES cells, and that human ES cells could be used for screening methods *in vitro* and the '659 document provide guidance with regard to the specific steps. Additionally, Elsea provide further guidance to show that various mouse models of human diseases, such as metachromatic leukodystrophy, do not produce a biochemical model that reproduces clinical symptoms (see Abstract) and therefore show a need in the art to produce cells that could be used for screening various human diseases using human cells.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 82-84, 96-98 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson *et al.* (**Science**, 282: 1145-1147, November 6, 1998) in view of Harper (**J. of Assisted Reproduction and Genetics**, 13(2): 90-95, 1996) in further view of US Pat. No. 7,390,659 (Issued June 24, 2008, cited previously) and Elsea *et al.* (**ILAR Journal**, 43(2): 66-79, 2002, cited previously) as applied to claims

52, 55, 58-60, 74, 75, 78-80, 85, 86, 88-94, 99, 100 and 101 above, and further in view of PGPub US 2005/0054092 A1. This rejection is maintained for reasons of record advanced in the prior Office actions (see Advisory Action, mailed 1/18/11; Final Rejection, mailed 7/30/10).

Rejection

Thomson, Harper, the '659 patent and Elsea are described above. They do not specifically teach isolating lineage specific cells by mechanical separation of cells tissues and/or tissue-like structures contained within the embryoid body. However, prior to the time of the claimed invention, the '092 document teaches that suspensions of pPS derived cells can be further enriched with desirable characteristics, such as mechanical separation or cell sorting (p. 8, ¶117). In particular, the '092 document teaches that FACS sorting can be used (p. 10, ¶144).

Accordingly, it would have been obvious for one of skill in the art to modify the methods taught by Thomson, Harper and Elsea, to include a step of isolating a lineage-specific cell, utilizing either cell sorting, such as FACS sorting, or mechanical isolation techniques, as taught by the '092 document with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to make this modification in order to have a purified population of cells for *in vitro* screening assays.

Claims 57, 81, 87, 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson *et al.* (**Science**, 282: 1145-1147, November 6, 1998) in view of Harper (**J. of Assisted Reproduction and Genetics**, 13(2): 90-95, 1996) in further view of US Pat. No. 7,390,659 (Issued June 24, 2008, cited previously) and Elsea *et al.* (**ILAR Journal**, 43(2): 66-79, 2002, cited previously) as applied to claims 52, 55, 58-60, 74, 75, 78-80, 85, 86, 88-94, 99, 100 above, and further in view of US Pat. No. 5,972,955. This rejection is maintained for reasons of record advanced in

the prior Office actions (see Advisory Action, mailed 1/18/11; Final Rejection, mailed 7/30/10).

Rejection

Thomson, Harper, the '659 patent and Elsea are described above. They do not specifically teach a sequence, such as those recited in claims 57, 81, 87 and 95. However, prior to the time of filing, the '995 reference teaches an exact match of SEQ ID NO: 24 (see alignment, presented previously).

Accordingly, it would have been obvious for the ordinary skilled artisan to modify the teachings of Thomson, Harper and Elsea, to screen for human embryos for a specific mutation, such as the W1282X as set forth in SEQ ID NO: 24, associated with cystic fibrosis, and use that embryo to produce an ES cell line, with a reasonable expectation of success. One of ordinary skill would have been motivated to make this modification in order to produce ES cells that could then be used for screen therapeutic agents for treatment of cystic fibrosis.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

This is a continuation of applicant's earlier Application No. 10/581,455. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (571)272-0736. The examiner can normally be reached on 9-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Thaian N. Ton/
Primary Examiner, Art Unit 1632